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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. |
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| 09/560,288 | 04/27/00 | HANLEY E | 8151-24A |

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| EXAMINER | |
|---|---|
| KERR, J | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1633 | 7 |

DATE MAILED: 05/09/01

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/560,288 | HANLEY ET AL. | |
| | Examiner | Art Unit | |
| | Janet Kerr | 1633 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *26 February 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *10,11,13-15 and 18-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10,11,13-15 and 18-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. § 119**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

**Attachment(s)**

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

### *Response to Amendment*

Applicants' amendment, filed 2/26/01, has been entered.

Claims 1-9, 12, 16, and 17 have been canceled.

Claims 10, 11, 13-15, and 18-34 are pending.

### *Claim Objections*

Claim 10 is objected to because of the following informalities: on line 3, the term "obtain" should be "obtained". Appropriate correction is required.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 10, 11, 13-15, and 18-34 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for the reasons of record and the reasons below.

The claims are directed to a therapeutic composition for use in treating human disc diseases, the composition comprising an implantation carrier in admixture with in vitro propagated human intervertebral disc cells claimed in a product-by-process format.

As stated in the previous Office action, the claims are not enabled as the specification does not provide sufficient guidance for one of skill in the art to provide the claimed composition which is therapeutically effective in treating human disc diseases. Moreover, the state of the art at

the time of filing teaches that treating human disc diseases with disc cells is neither routine nor predictable.

Applicant's arguments filed 2/26/01 have been fully considered but they are not persuasive. With respect to Issue 1, regarding the phenotype of cells in the therapeutic composition, it is argued that the implant cells were derived from the annulus of an adjacent sand rat disc and the cultured cells became de-differentiated based on morphology of the cultured cells. This is not persuasive as claimed invention is directed to human cells which are obtained from intervertebral disc tissue. It is not readily apparent from the claims or the specification whether the human cells are annulus or nucleus cells or whether the cells required for implantation are proliferative or differentiated cells. Applicants refer to the teachings of Wolmsley, Taylor *et al.*, and Ghosh to describe the derivation of disc cells during human development and further rely on Errington *et al.* who teach that the derivation of intervertebral disc cells are not known. These arguments are not persuasive as they do not address the issue of the human cell type obtained from expansion of disc tissue in vitro which is required in the therapeutic composition for use in treating human intervertebral disc diseases.

With respect to Issue 2, directed to whether the cells in the therapeutic composition are dedifferentiated, proliferating cells, or whether the cells are differentiated and secreting an extracellular matrix that is representative of the matrix observed in a normal intervertebral disc *in vivo*, it is argued that there are no commercial antibodies with which the matrix surrounding the labeled engrafted cells can be assessed. It is indicated that since matrix is elaborated by the cells native to the disc, this provides evidence that cells were making the appropriate matrix. These arguments are not persuasive. As stated in the previous Office action, the type of matrix elaborated by disc cells is dependent on the type of disc cell and the environment of the cells. Aigner *et al.* teach that the disc contains three regions, each of which differ in composition, and Guilak *et al.* teach that intervertebral disc tissue comprises a heterogeneous population of cells which have distinct biosynthetic capacities and which respond to stimuli differently. As the population of cells and the synthetic capacity of the cells of the instant invention are not defined, it

is not readily apparent that the therapeutic composition of the instant invention can reproducibly and consistently be effective in treatment of generally claimed intervertebral disc diseases.

With regard to Issue 4, regarding the unpredictability of using the therapeutic composition of the instant invention for treating human intervertebral disc diseases, it is argued that the reference of Aigner *et al.* discusses cells within the endplate and the endplate is composed of cartilage, not disc tissue. This is not persuasive. Aigner *et al.* was relied upon to teach that the intervertebral disc consists of three regions, that the three regions each have a distinct organization and composition. Given the heterogeneity of disc architecture and composition, and the lack of teachings in the specification as to which cell type is required for implanting such that the appropriate matrix is elaborated and is therapeutically effective in treating disc diseases, it would require undue experimentation to make and use the invention as claimed.

With regard to extrapolating *in vivo* results from animal models to humans, it is argued that the two references relied upon, Frick *et al.* and Luk *et al.*, are directed to disc transplantation, not cell implantation and thus, the references are not relevant to the claimed invention. This argument is not persuasive. The references were relied upon to teach that treatment of intervertebral disc diseases by providing tissue to the damaged area is neither routine nor predictable as the extent and the effectiveness of the regenerative process is still unclear and requires further studies. Moreover, both references clearly state that while animal models are suitable for studying the effects of different therapeutic regimens for treating disc diseases, the skilled artisan cannot extrapolate results from these animal models to humans. Given the lack of a working example in which implantation of the claimed therapeutic composition provides therapeutic efficacy in treating human intervertebral disc cells, the lack guidance as to the types of cells and the state of differentiation of the cells provided in the therapeutic composition, the unpredictability in the art with respect to therapeutic effectiveness of tissue-based treatments for intervertebral disc diseases, and the lack of prior art teachings of cell-based treatment regimens for intervertebral disc diseases, it would require undue experimentation to make and use the

therapeutic composition as claimed. Thus, for the reasons of record, and the reasons stated above, the rejection is maintained.

It is indicated that several references relied upon in applicants' Response have been enclosed. However, no references were attached to applicants' Response. The examiner will consider these references upon receipt.

**THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet M. Kerr whose telephone number is (703) 305-4055. Should the examiner be unavailable, inquiries should be directed to Deborah Clark, Supervisory Primary Examiner of Art Unit 1633, at (703) 305-4051. Any administrative or procedural questions should be directed to Kimberly Davis, Patent Analyst, at (703) 305-3015. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 305-7401.

Janet M. Kerr, Ph.D.
Patent Examiner
Group 1600

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